

Cardiac surgery — An offspring of experiment

M. S. Valiathan

Cardiac surgery is like a drama which is still unfolding. Old scenes of conflicting ideas, procedures and technologies give place to the new in quick succession leaving nothing unchanged on the stage.

While accepting the honour of giving the C. V. Raman Memorial lecture, I had the unflattering notion that he would have regarded medicine and surgery as no more than crafts and surgery, in particular, as a variant of hewing wood and drawing water. Little did I know that Prof. Raman had clearly foreseen the importance of the active borderland between physics and medicine. He had even dreamt of building an Institute of Medical Physics complete with attached hospitals! I am grateful to Prof. Ramaseshan for the following extracts from the Raman archives.

'It is considered to be highly desirable that the future activities of the Raman Research Institute may be directed into a new channel, viz. study and research in the borderline areas between physics and medicine. There is extensive scope for work in this field which could lead both to fundamental advances in scientific knowledge and to developments of importance in medical practice. ...to the development of an Institute of Medical Physics with the necessary laboratory and library facilities, as well as the attached hospitals and staff residences'.

In lighting up the borderland between physics and medicine with his powerful mental searchlight, Prof. Raman anticipated interdisciplinary research long before its time. Nothing of importance or interest in science escaped his keen eye.

Cardiac surgery is a new entrant in the field of surgery. Its birth dates back to no earlier than the nineteen forties. But unlike general surgery which took twenty centuries to reach the present level of excellence, cardiac surgery leapt from infancy to adulthood in less than fifty years. It marched to the beat of an altogether different drum. What powered the giant leap was the ethos of experiment which underpinned every major development in cardiac surgical history. As a supreme experimentalist, Prof. Raman, I believe, would have looked upon cardiac surgery with approval.

Evolution of surgery

The origins of surgery are lost in the mists of antiquity. The discovery of trephined skulls and amputated limbs in archaeological excavations suggest that the cave-men did practise surgery with sharp instruments of flint. A thousand years before the Buddha, the *Atharva Veda* referred to the removal of arrows from the body and the passage of catheters for urinary retention; but the procedures were no more than elements in an elaborate ritual which emphasized incantations and amulets. A hundred years before the Buddha, however, the surgical scene changed dramatically in India. Superior instruments made from iron appeared and extended the scope of surgery even as the knowledge of anatomy, physiology and pharmacology advanced. But the heroic age of surgery which saw the rise of master surgeons like Sushruta and Jivaka was followed by a mysterious decline which is evident in many subsequent texts. Sushruta's techniques were hardly taught or practised by the time of the *Ashtanga Hridaya* of the 7th century A.D. Europe, on the other hand, had no Sushruta and its surgery, such as it existed, was practised by barbers with disastrous results until the eighteenth century. For good measure, the surgeons in the German army in the 15th and 16th centuries were required to shave their men as part of their duties! The general gloom was only lightened in part by shining figures like Ambrose Pare in the 16th century. Progress in surgery, as we know it today, did not begin in Europe till the 18th century; nor did it pick up momentum until the 19th.

Three circumstances combined to reduce the global advance of surgery to a slow and hesitant march. In the first place, surgical progress was totally dependent on empiricism. If skulls were trephined to let out evil spirits, it took centuries for the practitioners to realize that more patients died from bleeding and infections following the procedure than from the fury of evil spirits. In historical times, when amputations carried a mortality of 70%, the polemics on the relative merits of turpentine, glycerine, iodine and technical skills in improving operative results raged for many years until Lister settled the issue by introducing antiseptics. The story of blood letting is no different. It had its proponents for centuries who swore by its undoubted

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benefits for patients with various illnesses. It was also claimed to assist in the recovery of patients following surgical operations. The controversy on blood letting took long to fade away; but its faint echo continues to be heard in the management of blue babies. Twentieth century too had its share of tragi-comedies which were vigorously advocated, only to be abandoned after many years. A few among the many examples are total dental extraction and colectomy for the removal of focal sepsis, tonsillectomy for sorethroat, sympathectomy for angina pectoris and gastric freezing for peptic ulcer. In each of these misadventures, the proponents never doubted their efficacy and scoffed at any suggestion for a controlled trial. Learning from trial and error—more error than trial in reality—cost a great deal in time and even more in human suffering.

Secondly, surgical progress was severely handicapped by the absence of anaesthesia which did not appear until the nineteenth century. In the pre-anaesthetic era, surgery was done on patients who were intoxicated or physically restrained. Speed was of the essence and surgeons like Astley Cooper completed a thigh amputation in three minutes! Thirdly, post-operative infection bedevilled surgical endeavour and unbarred the gates to the hell of complications and death. Indeed, it was the post-operative mortality of 70% following amputations which stung Lister's conscience and led to his development of antiseptics by carbolic spray. Freed from the constraints of anaesthesia and antiseptics, surgery did advance rapidly in the twentieth century; but empiricism persisted as old habits die hard.

Entry of cardiac surgery

Cardiac surgery was lucky to be born with the rich inheritance of anaesthesia, asepsis and the time-tested techniques of surgical reconstruction. On these foundations it built a marvellous edifice whose plan was obtained from experiment and building materials from physical, chemical and engineering sciences.

Consider, for example, the management of 'blue babies'. In its commonest variety named after a French physician Fallot, the connection between the right ventricle and pulmonary artery is severely narrowed with the result the children suffer from poor oxygenation of blood. The problem is compounded by a large hole in the wall between the right and left ventricles and the shunting of venous blood from the right to the left chamber (Figure 1). Until the late nineteen forties, little could be done for these very sick children who were often quite intelligent, lack of oxygenation of the brain notwithstanding. Around this time Blalock—one of the founders of cardiac surgery—was attempting to overcome the congenital narrowing of aorta or coarctation by turning down a branch from above the narrow segment



Figure 1. Fallot's anomaly.

to the aorta below in experimental animals (Figures 2 and 3). When he reported his results, Taussig—his opposite number in pediatric cardiology—wondered why the branch could not be connected to the pulmonary artery to augment the flow of blood to the lung. Blalock worked on her suggestion in the Hunterian laboratory of the Johns Hopkins and perfected the technique over innumerable experiments. It was clear to him that the new connection would significantly enhance the blood flow to the lung. Thus was born the famous Blalock—Taussig operation which changed the outlook for these children and laid the foundations of pediatric cardiac surgery (Figure 4). The experimental work of Blalock not merely gave birth to a new surgical technique; it also stimulated further studies on the circulatory physiology of Fallot's anomaly and its alteration by the Blalock—Taussig operation. Above all, it established a pattern which was to be triumphantly replicated many times in the history of cardiac surgery. The pattern consisted of a clinical problem for which a physiological or mechanical solution was suggested: the solution was worked out in turn in the experimental laboratory and brought back to the bedside for clinical application months or years later.

Hardly five years had passed after Blalock's operation when Hufnagel startled the world by inserting a ball



Figure 2. Coarctation of aorta.

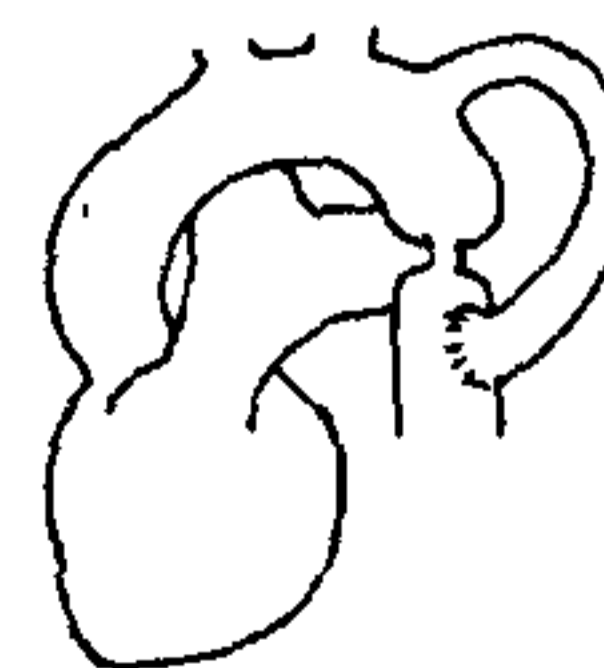


Figure 3. Coarctation of aorta, attempted procedure.



Figure 4. Blalock-Taussig procedure.

valve in the thoracic aorta for the treatment of aortic regurgitation. Hufnagel was a great experimenter whose outlook on medicine, science and life was greatly influenced by the legacy of Alexis Carrell. It was none other than Hufnagel who deposited the Carrell papers in the Georgetown University Library. In the late nineteen forties, he too was working in the laboratory at Boston for relieving coarctation of aorta which had already drawn the attention of Blalock in Baltimore. However, Hufnagel's approach differed radically from Blalock's in so far as it sought to replace the narrowed segment of the aorta with a tube of polymethyl methacrylate (PMMA). As early as 1942, he had shown that the tubes would remain patent in the thoracic aorta of dogs for prolonged periods of time (Figure 5). He soon convinced himself that placing a ball valve of PMMA in the same position would correct aortic regurgitation from regions distal to the valve. He was not deterred by objections including the fact that a valve in the thoracic aorta would leave the regurgitation from the arteries of the head and arms uncorrected. When he developed a ball valve of PMMA and established the technique of its quick insertion in the laboratory he lost no time in implanting it in a patient with severe aortic regurgitation for which no effective treatment existed in 1952. The patient improved dramatically to the surprise of critics and delight of relatives (Figure 6). It was left to a physiologist like Sarnoff to quantify the volume of regurgitant flow which was controlled by the valve and establish the physiologic basis of its success. If Blalock's technique clothed a physiological idea, Hufnagel's valve drew upon the combined resources of physiology, materials science and fabrication technology. Given the

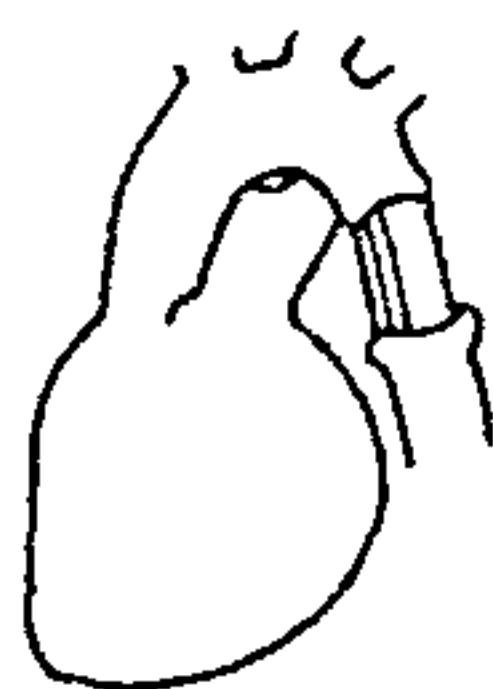


Figure 5. Intubation of thoracic aorta.

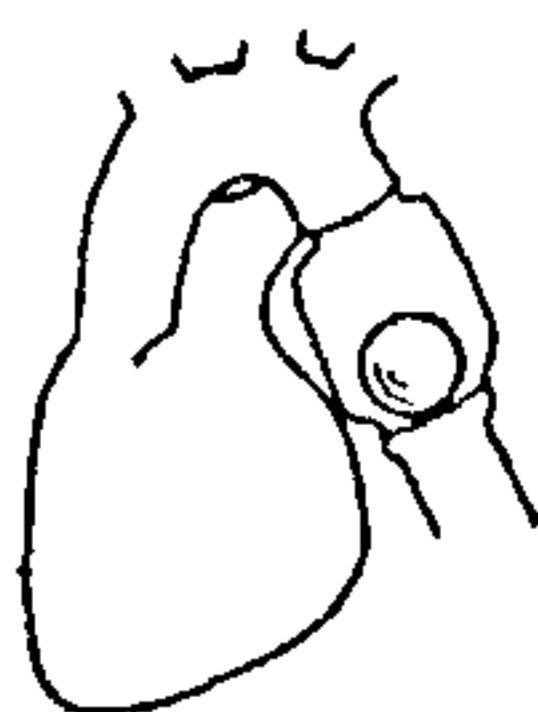


Figure 6. Ball valve in the thoracic aorta

entry of the science and technology in full force, cardiac surgery was never the same again.

Surgical procedures on the pulmonary artery and aorta were one thing; operation inside the heart under vision was quite another. This was the dream which animated Gibbon when he, as a medical student, watched a patient die from a massive clot in the pulmonary artery. The patient had no signs of systemic disease and his vital organs were normal—yet a clot from the leg had literally shot him from within. If only the heart and lungs could be switched off for a few minutes, dreamt young Gibbon, the clot could be easily removed and the heart chambers inspected for extra clots. Gibbon's encounter took place around 1930 when any mention of heart-lung bypass would have been dismissed as scientific rubbish. But Edward Churchill encouraged him, the surgeon-philosopher that he was. Gibbon sought to develop a film oxygenator in the place of lung by gently spreading venous blood over a solid surface and exposing it to an atmosphere of oxygen to facilitate gas exchange. It was to the credit of Gibbon that he observed that an irregular support, such as a wire-mesh screen, would cause a gentle turbulence in the bloodfilm and thereby promote continuous admixture between the inner and outer layers of the film. This was essential to overcome the barrier posed by the saturated outer layer. The oxygenated blood was put back into the patient by a pump which was simple and robust. The development of the Gibbon heart-lung machine took over twenty years when his only associates were Mary Gibbon and the IBM engineers who shared his conviction and enthusiasm. Gibbon brought the machine from the laboratory to the operating room in Philadelphia in 1953 to close a hole in the heart of a patient under vision. That was a historic event because it marked the birth of open heart surgery which took the world of medicine by storm. If open heart operations the world over approach 400,000 a year today and offer effective relief to patients ranging from the new born to the octogenarian, we owe much of it to the endeavour of Gibbon.

In more recent times, Gott's discovery of the Graphite-Benzalkonium-Heparin coating (GBH) made the surface of rigid materials clot-free without altering their mechanical properties and triggered an impressive effort in the development of blood compatible materials. In trying to develop a leaflet valve with a polymethyl methacrylate housing Gott coated the plastic with colloidal graphite in the belief that the semiconductivity of graphite would inhibit thrombus formation. The graphited plastic rings did stay thrombus-free, but it was much later that Gott and colleagues realized that resistance to thrombosis was not so much a property of graphite as that of its sequential soaking in benzalkonium chloride and heparin. The ionic bonding of

heparin which Gott discovered was a major contribution to biomaterials science, quite apart from its applications in techniques such as heparinised shunts for thoracic aortic bypass. His work demonstrated once again the spell of the laboratory over cardiovascular surgery.

Absorption of science and technology in cardiac surgery

If the philosophy and method of experiment permeated its development, cardiac surgery turned to science and technology for its tools and techniques. Support came from an astonishing variety of disciplines—physiology, materials science, electronics, chemical engineering and biostatistics—to name just a few. Their impact spared no aspect of cardiac surgery which absorbed more of science and technology than any other branch of medicine. Heart-lung bypass which underlies all open heart surgery, physiological correction of congenital anomalies, replacement of damaged parts, assist techniques for a failing pump and transplantation for end-stage-disease—these and other procedures illustrate the role of science and technology in shaping the practice of cardiac surgery. The following are no more than examples.

Heart-lung bypass—oxygenation sans lung

Blood oxygenator—the centrepiece of the heart-lung machine — has come a long way since Gibbon. In the place of a bulky instrument which demanded large volumes of blood for priming and remained difficult to clean and operate, the oxygenators of today are highly efficient, low in priming volume and sleek in appearance. Those in current use rely either on the bubble principle or a membrane across which gaseous diffusion occurs.

While membrane oxygenators are more physiological, their cost is prohibitive and bubble oxygenators continue to dominate the market. In the bubble oxygenator developed by the Sree Chitra Tirunal Institute (Figure 7), the central chamber consists of a chimney in which venous blood ascends while oxygen bubbles through the column (Figure 8). The venous blood gives up carbon dioxide and picks up oxygen thanks to the high affinity of hemoglobin for oxygen. The frothy, oxygenated blood then cascades over a large area of defoaming substrate in the next concentric chamber. The defoamed, oxygenated blood settles in turn in the outermost, arterial chamber from where it is pumped back to the patient. The bubble chimney also incorporates a heat exchanger which permits elective cooling or warming of the patient (Figure 8). Successfully tried in several centres, the oxygenator will



Figure 7. SPICTRA oxygenator

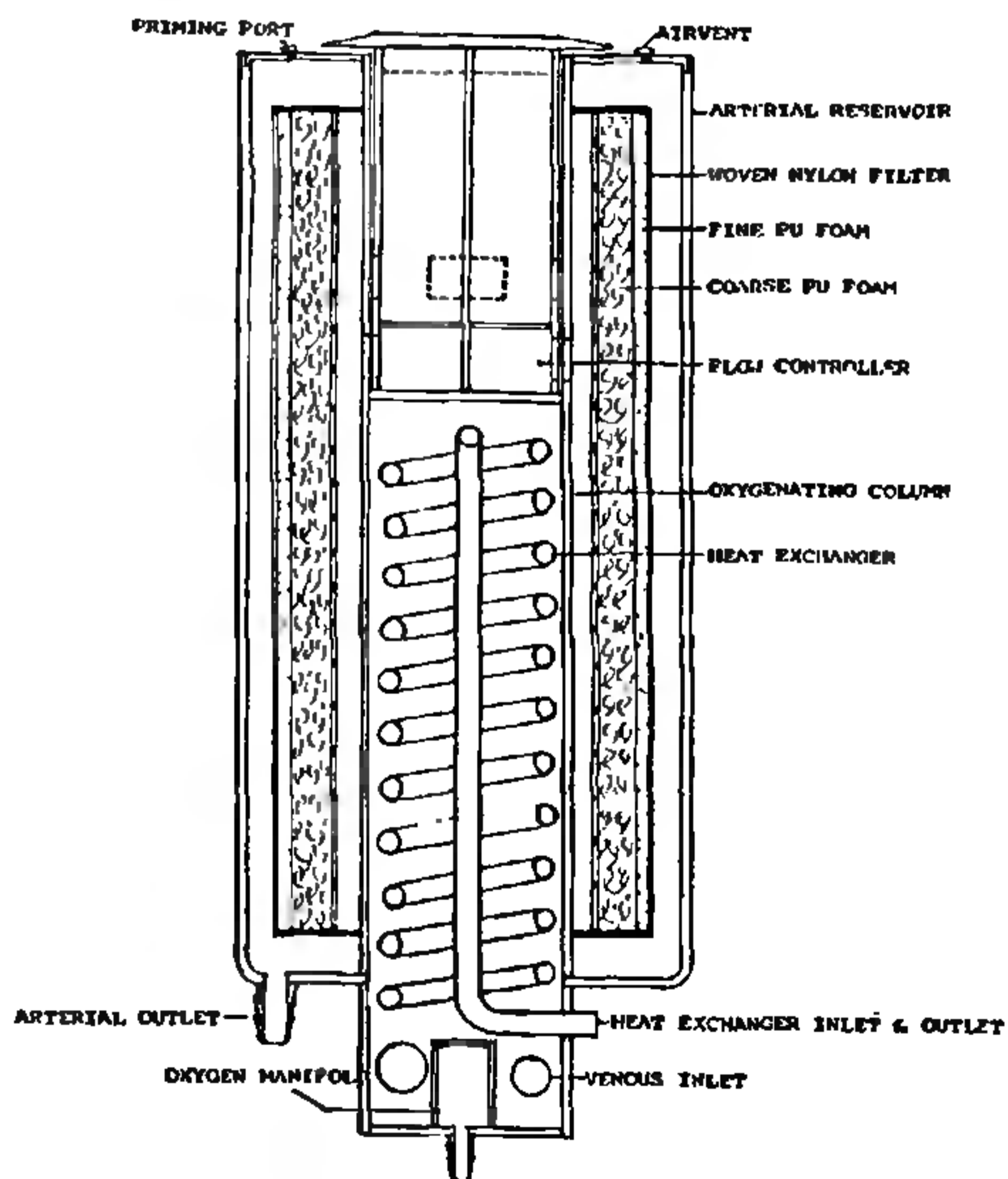


Figure 8. SPICTRA oxygenator, section.

soon be commercially produced. In construction, it employs over a dozen polymeric materials which are biocompatible; the bubbler features a mixture of coarse and fine pores to optimise the bubble population and oxygen transfer; and the unit takes advantage of the fact that a large gas-blood contact surface can be created in a relatively small amount of blood by bubbling oxygen through it. The experience in developing a bubble oxygenator is a necessary input for the development of more advanced systems for blood-gas exchange which will support lung function for considerably longer periods.

Physiological correction of congenital anomalies

Congenital anomalies of the heart occur at the rate of 4-5 per thousand births and vary widely in complexity. Many of them involve the misplaced connection of large veins to the receiving chambers, wrong connection of the receiving chambers to the pumping chambers or the faulty association of the pumping chambers with the great arteries. There is however a method in the madness of these faulty connections which occur with singular regularity. They are not diseases in the conventional sense and Taussig even suggested that they are reminders of the failed models of cardiac evolution when reptiles differentiated into mammals.

While several congenital anomalies are corrected by surgical repair and restoration of near-normal anatomy, others are too complex for a direct approach. An example is a condition where cardiac anatomy is normal except that the aorta and pulmonary artery are connected wrongly to the right and left ventricles (Figures 9 and 10). As detaching the arteries and connecting them to the appropriate chambers were hazardous and slow to gain acceptance, an ingenious technique was invented by Senning who switched the atria in such a manner that the venous and arterial

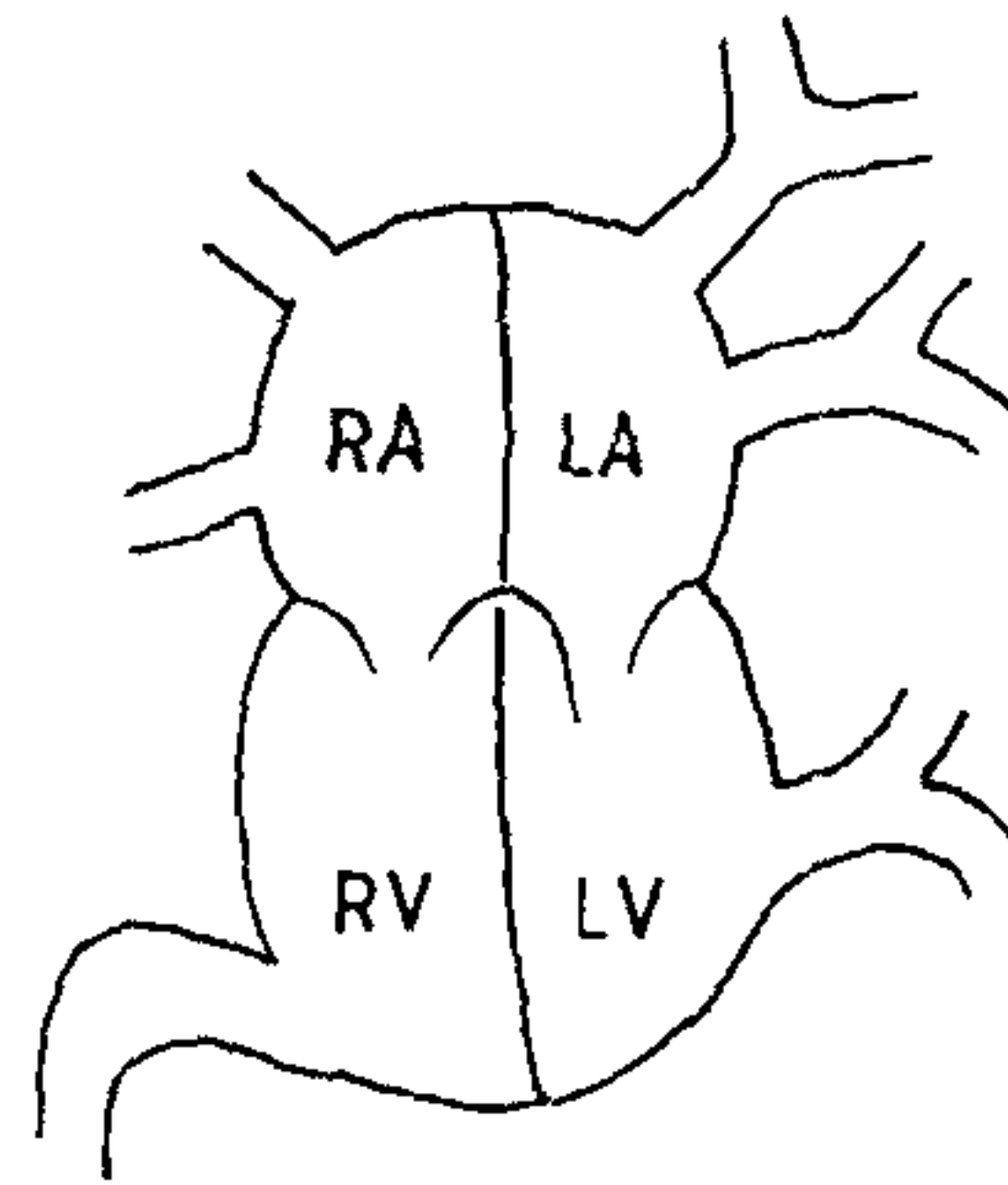


Figure 10. Transposed connections of pulmonary artery and aorta.

blood flowed to the 'wrong' ventricle (Figure 11). This was surely one instance of two anatomical wrongs making a physiological right to the immense benefit of sick children. The Senning operation was a physiological experiment which posed numerous questions. Designed to support a low pressure, pulmonary circulation, will the right ventricle sustain the sudden load of the high-pressure, systemic circulation? Will the tricuspid valve meant for guarding a low pressure chamber withstand the sudden rise in pressure in the right ventricle? Time provided the answers and vindicated Senning who literally breathed new life into these children.

Replacement of diseased parts

For all their marvellous design and construction, cardiac structures like valves and physiological pacemaker do become irreversibly damaged by disease and demand replacement. Since the time of Hufnagel's historic valve in the descending thoracic aorta, a large

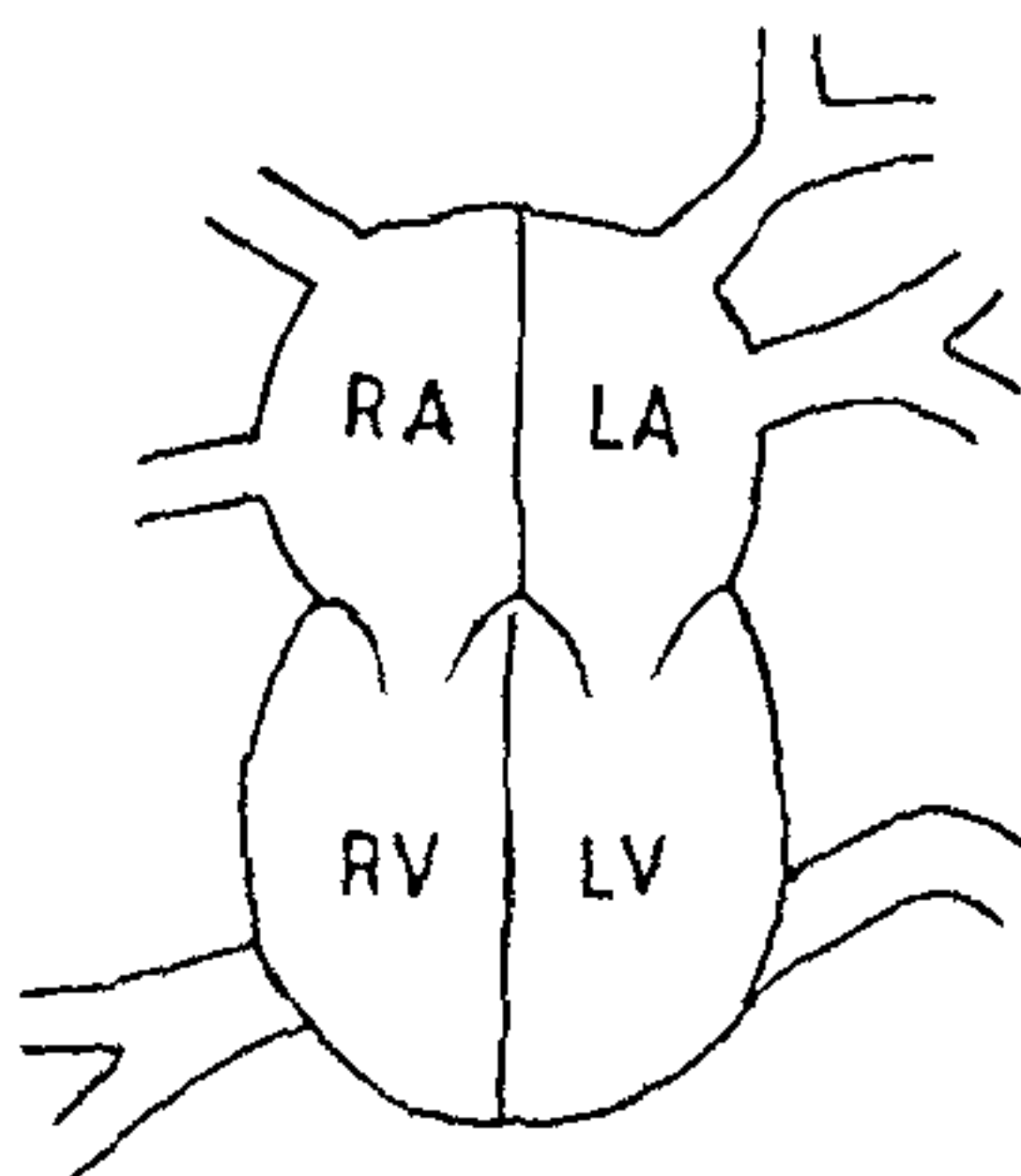


Figure 9. Normal connection of pulmonary artery and aorta

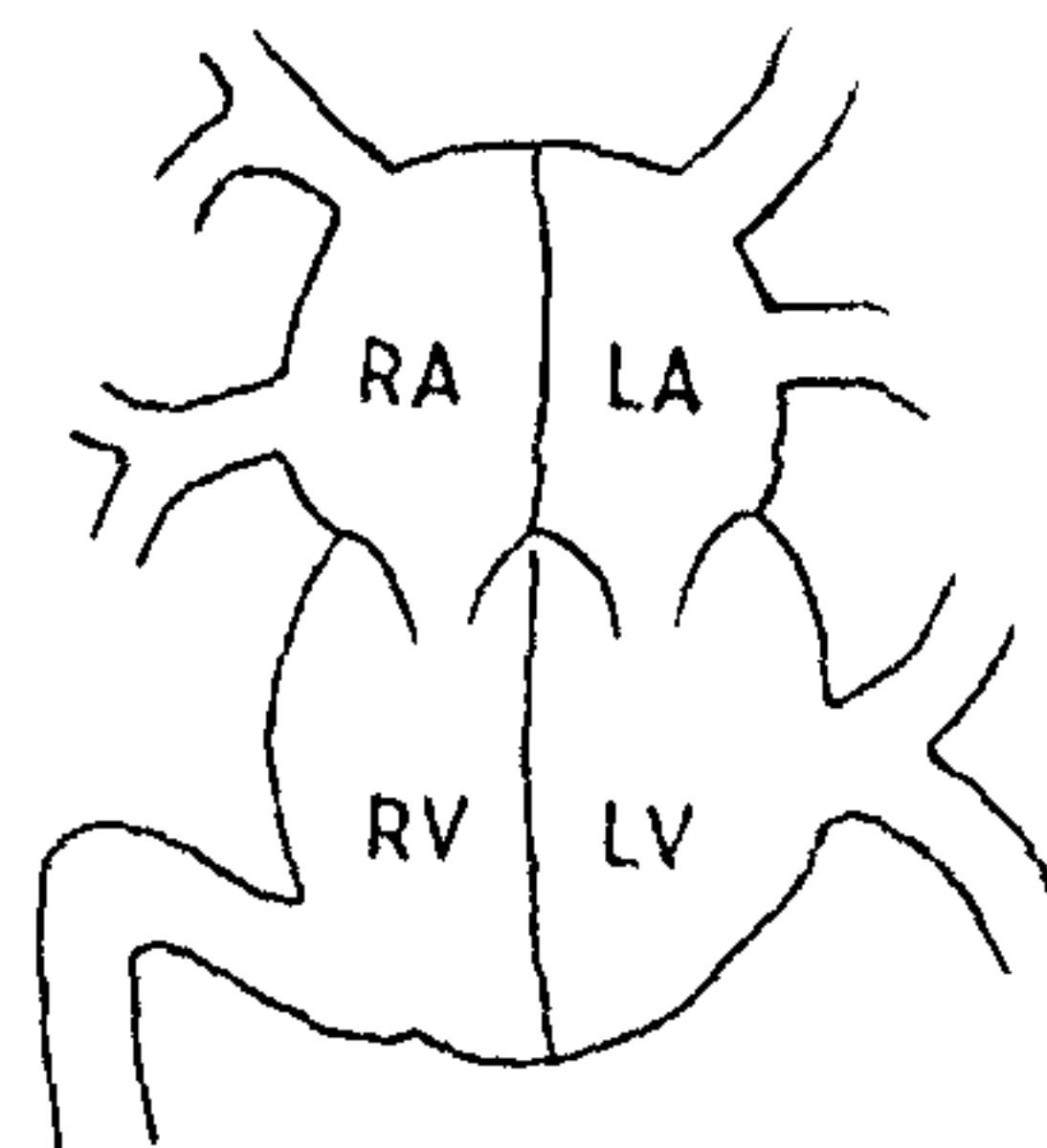


Figure 11. Physiological correction by Senning

GENERAL ARTICLES

number of mechanical and tissue valves have been developed and used for the intracardiac replacement of diseased valves. While the replacement of badly damaged valves has enabled hundreds of thousands of patients to return to productive lives, no valve is perfect and each model has its own share of merits and demerits. The bottom line is that all patients with artificial valves need medical surveillance for life.

Under successful clinical trial, the Chitra valve belongs to the class of mechanical valves and has a decade of development behind it (Figure 12). Its housing is made of Haynes alloy 25, the disc occluder from ultra-high-molecular-weight polyethylene and sewing ring from polyester cloth. Apart from ensuring that the component materials are biocompatible and possess the requisite engineering properties, it is essential that the valve prototype passes elaborate tests for hydraulic function and durability before being tried even in animals. A prosthetic valve illustrates, as few other devices do, the crucial role of materials science and advanced machining technology in the day-to-day work of cardiac surgery.

Pacemakers are something else again. A small cluster of specialized cells pace the heart at a rate characteristic for each species. This cluster or pacemaker paces the heart of a humming bird at 500 per minute and that of a turtle at 15 to suit their metabolism and life style. The human heart throbs in between and its pacemaker fires at the rate of 70–80 per minute at rest. When it fails, the rate may drop as low as 30 at which level the pumping of the heart is no longer effective. An artificial pacemaker has a pulse generator which consists of lithium cells for energy source, a microchip to regulate the rate and encasing materials to seal the unit hermetically. Implanted beneath the skin, the pulse

generator weighs no more than 50 g and establishes contact with the heart through an electrode wire which transits through a large vein in the neck. Made of alloys like elgiloy with excellent ductility the wire is ensheathed in biocompatible plastics like polyurethane. Since the electrode tip is anchored in the heart muscle, the hook-up is more-or-less permanent and the pulse generator may not need a change for as long as 15 years. Though nowhere in elegance or miniaturisation before nature's little cluster of cells, man-made pacemakers have saved countless lives from the hands of the Grim Reaper.

Cardiac-assist techniques

When the contractility of heart muscle dwindles all of a sudden and the pump fails due to reversible causes, it is imperative that the heart is assisted and given time for recovery. This grave situation arises following major heart attacks when large areas of heart muscle are deprived of blood supply, or operations which cause a temporary set-back to cardiac function. A surgeon and an engineer – Harken and Birtwell – noted that the heart muscle could be assisted by reducing the after-load and increasing its blood supply, which correspond to the ejection and relaxation phases of the cardiac cycle. They developed an imaginative technique called counter-pulsation to achieve the twin goals of cardiac assist. A balloon introduced into the thoracic aorta through a peripheral artery was triggered by the electrocardiogram to inflate during cardiac relaxation to enhance coronary arterial flow, and deflated during ejection to reduce cardiac after-load (Figures 13,14). Helium was used to produce quick inflation and deflation of the balloon

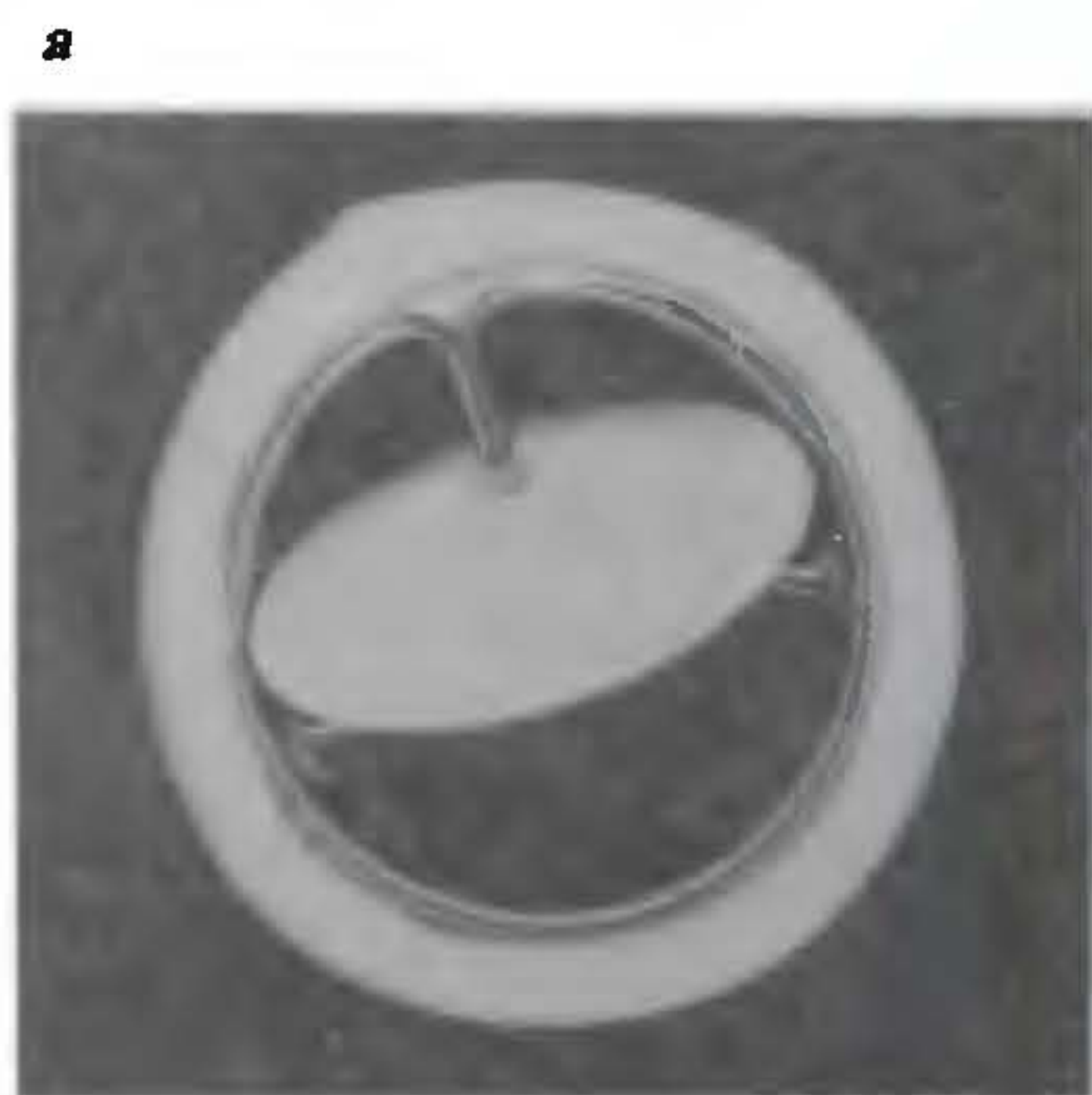


Figure 12. *a*, Chitra valve *b*, The Chitra valve is shown open in the aortic position of a patient whose diseased valve has been excised. Developed at the Sree Chitra Tirunal Institute, Thiruvananthapuram, the valve consists of a housing of Haynes -25 alloy, disc of ultra-high-molecular-weight polyethylene and sewing ring of polyester. Clinical results have confirmed the excellent hydraulic characteristics of the valve.

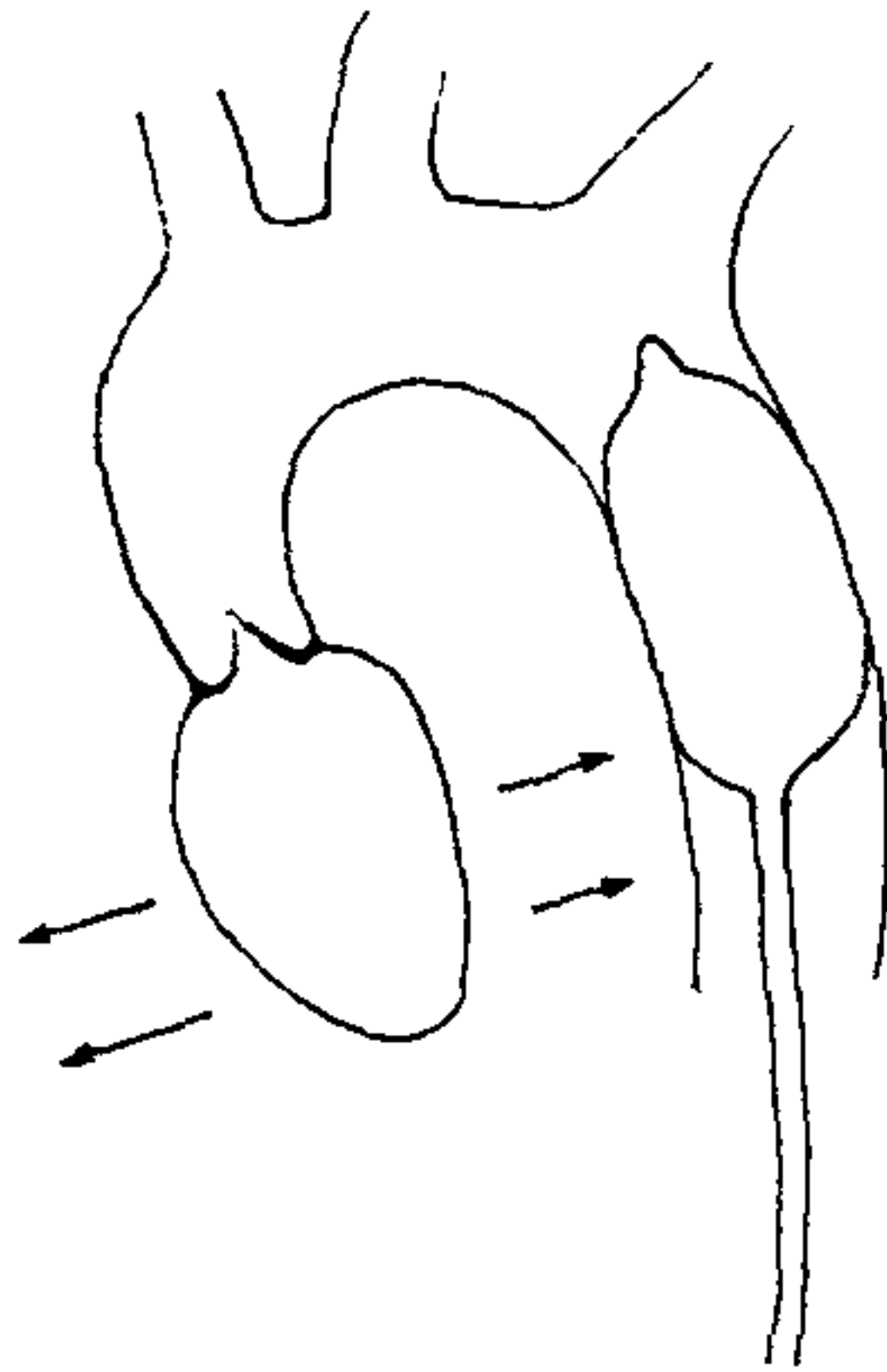


Figure 13. Intra-aortic balloon during cardiac relaxation.

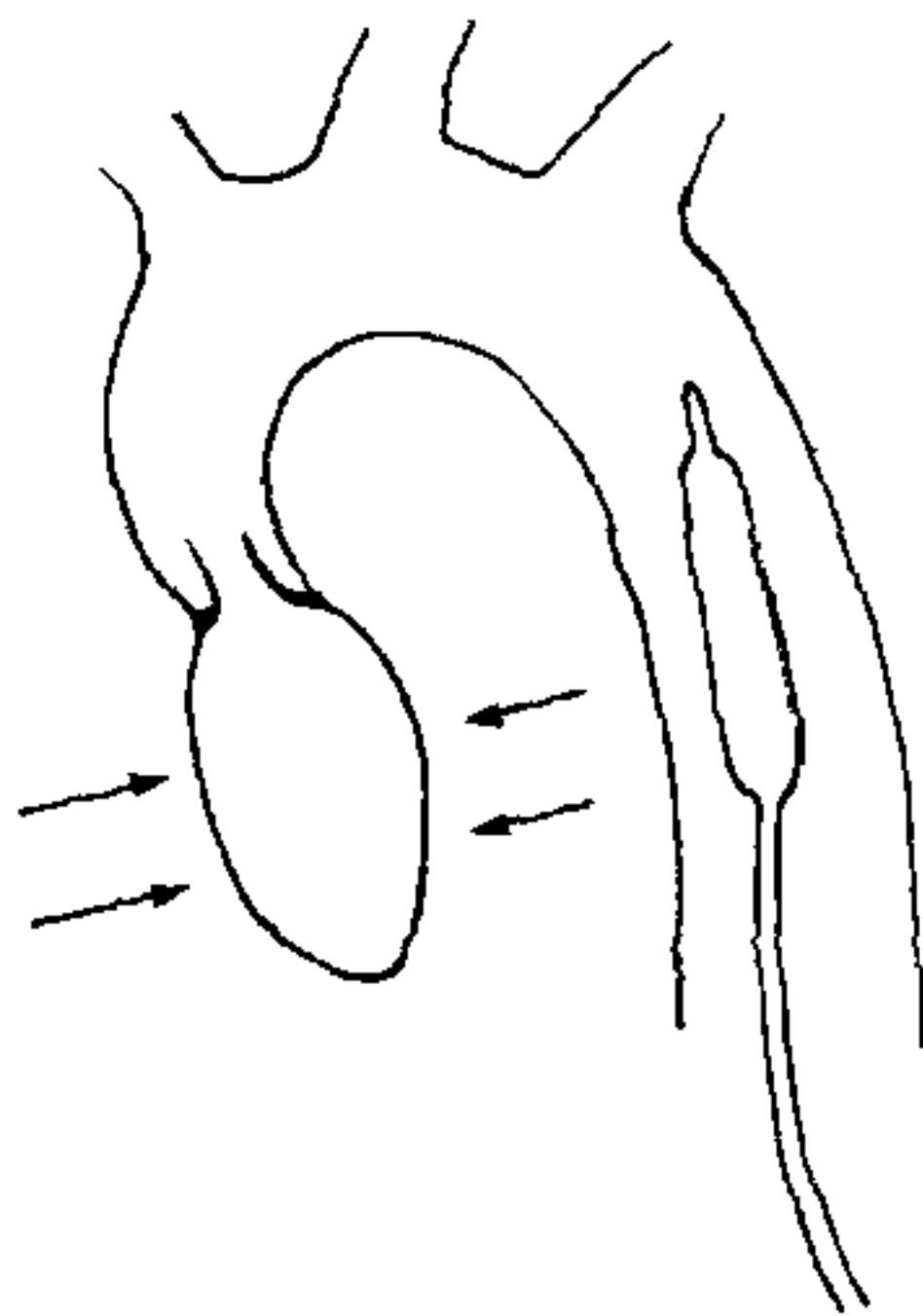


Figure 14. Intra-aortic balloon during cardiac ejection.

which was made of segmented polyurethane. Counterpulsation by intra-aortic balloon is a standard technique which is indispensable for the management of many a cardiac crisis today. Cardiac assist techniques including the intra-aortic balloon represent a triumphant synthesis of contributions from physiology, electronics and mechanical engineering.

Cardiac transplantation

When muscle disease or recurrent ischemic attacks wreck the pumping function of the heart the sole hope for survival lies in transplantation of the heart. The classic observations of Medawar and Burnet on tissue

immunity and the practice of kidney transplantation for two decades notwithstanding, immunology began to quiver with excitement only from 1968 when Barnard transplanted the heart in a patient. Thanks to the patient and meticulous work of many groups and the advent of cyclosporin-A, cardiac transplantation is well-established today with 70% survival at 5 years. Apart from salvaging patients on the verge of death, cardiac transplantation uncovered new ground in HLA typing, organ preservation, immunologic rejection and tolerance, immunosuppression and immunologic triggering of atherosclerosis. The shortage of donor hearts even led to the redefinition of the criteria of death in many countries!

Prior to cardiac transplantation in man, experimental work had been in progress for decades on transplanting the heart as a replacement in the chest, or as a supplemental pump elsewhere in the cardiovascular system. One has only to look at the painstaking and methodical work of Shumway at Stanford who tried to perfect immunosuppression in a colony of dogs with transplanted hearts before Barnard's achievement. The untold story is that of Alexis Carrell who anticipated the present event long ago when he relocated kidneys and heart in the neck experimentally by establishing vascular connections. If the mechanisms of immunosuppression were an outcome of basic research in immunology the technique of transplantation owed no less to laborious years of work in the laboratory.

Conclusion

Reared by experimental science, the drama of cardiac surgery is still unfolding. In this drama sans direction, old scenes of conflicting ideas, procedures and technologies give place to the new in quick succession and leave nothing unchanged on the stage. The contrary processes of abrogation and affirmation, demolition and reconstruction alternate as the act progresses in an atmosphere of increasing expectancy and hope. This is no melodrama because abrogation and affirmation in cardiac surgery are products of carefully designed experiments which bear the heavy imprint of biostatistics. To note the statistical rigour of studies on coronary artery bypass or valve replacement is to recognise how far cardiac surgery has moved from empiricism toward the status of a truly scientific discipline.

The enterprise of cardiac surgery also resembles a grand mansion with many large and sunlit rooms which are transient witnesses to an effort without end. At all times, parts of the mansion are under remodelling and all parts are under remodelling sometime. The plans for the new models derive inspiration from the changing milieu, climate, hazard function of occupants and other shifting episodes of human existence. Building materials

too change to suit the evolving style of architecture which itself fades away in ten or twenty years. But the rebuilding is scarcely possible without the preexisting structure as the old is the very means for us to come upon the new. We are nothing without our predecessors, yet we are more.

Beneath the magic mansion, however, is a permanent foundation which age does not wither nor change consume. The foundation draws its permanence from

compassion to fellow-humans and the search for wisdom which lend substance and meaning to all human endeavour. So long as the foundation lasts, it will support the edifice for all seasons, however mighty and moveable it may be. Charaka said that the practice of medicine is neither for self-aggrandisement nor for pleasure, but for the sake of compassion to fellow humans. Twenty centuries later, cardiac surgery can say that again.
